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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/483,434	01/14/2000	JEFFERY L. MILLER	14014.0360	8390
36339	7590	03/04/2004	EXAMINER	
NATIONAL INSTITUTE OF HEALTH C/O NEEDLE & ROSENBERG, P.C. SUITE 1000 999 PEACHTREE STREET ATLANTA, GA 30303			LEFFERS JR, GERALD G	
			ART UNIT	PAPER NUMBER
			1636	

DATE MAILED: 03/04/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

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Office Action Summary

Application No.

09/483,434

Applicant(s)

MILLER ET AL.

Examiner

Gerald G Leffers Jr., PhD

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 02 February 2004.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 3,9 and 10 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 9 and 10 is/are allowed.
- 6) ☒ Claim(s) 3 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- ☒ Notice of References Cited (PTO-892)
- ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____
- ☒ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____
- ☐ Notice of Informal Patent Application (PTO-152)
- ☐ Other: _____

DETAILED ACTION

Receipt is acknowledged of an After-Final amendment, filed 2/2/2004, in which claims 7 and 18 were cancelled. This amendment has been entered into the file, as it does not raise new issues. Claims 3, 9 & 10 remain pending and are under consideration in the instant application. For the following reasons, prosecution in this application is hereby reopened.

In the Final Action mailed 10/1/2003 the examiner made a request that applicants provide a copy of a meeting abstract from 1997 co-authored by at least two of the instant inventors. It is noted that applicants did not respond to the examiner's request in any way in the After-Final response filed 2/2/2004. The request is summarized below.

Relevant Art

The following reference appears to be relevant art for examination of the pending claims, but the examiner has not been able to obtain a copy of the reference. As the authors of this work appear to be two of the inventors of the instant specification, it is requested that applicants provide a copy of the reference. The reference is as follows:

Wojda, U., Miller, J. L. "Endocytosis mediated by biotin-avidin crosslinking of surface proteins does not require Gpl-proteins" Molecular Biology of the Cell (November 1997), Vol. 8, No. SUPPL., page 86A.

However, the examiner was able to obtain a copy of the meeting abstract in the interim and the reference is relevant art to the invention of claim 3. In fact, the reference is anticipatory of the invention recited in claim 3 (see the rejection below made under 35 U.S.C. 102(b)). Applicants are reminded of their duty to disclose relevant prior art under 37 C.F.R. 1.56, which is repeated below:

§ 1.56 Duty to disclose information material to patentability.

(a) A patent by its very nature is affected with a public interest. The public interest is best served, and the most effective patent examination occurs when, at the time an application is being examined, the Office is aware of and evaluates the teachings of all information material to patentability. Each individual associated with the filing and prosecution of a patent application has a duty of candor and good faith in dealing with the Office, which includes a duty to disclose to the Office all information known to that individual to be material to patentability as defined in this section. The duty to disclose information exists with respect to each pending claim until the claim is cancelled or withdrawn from consideration, or the

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application becomes abandoned. Information material to the patentability of a claim that is cancelled or withdrawn from consideration need not be submitted if the information is not material to the patentability of any claim remaining under consideration in the application. There is no duty to submit information which is not material to the patentability of any existing claim. The duty to disclose all information known to be material to patentability is deemed to be satisfied if all information known to be material to patentability of any claim issued in a patent was cited by the Office or submitted to the Office in the manner prescribed by § 1.97(b)-(d) and 1.98. However, no patent will be granted on an application in connection with which fraud on the Office was practiced or attempted or the duty of disclosure was violated through bad faith or intentional misconduct. The Office encourages applicants to carefully examine:

- (1) Prior art cited in search reports of a foreign patent office in a counterpart application, and
- (2) The closest information over which individuals associated with the filing or prosecution of a patent application believe any pending claim patentably defines, to make sure that any material information contained therein is disclosed to the Office.

(b) Under this section, information is material to patentability when it is not cumulative to information already of record or being made of record in the application, and

- (1) It establishes, by itself or in combination with other information, a prima facie case of unpatentability of a claim; or

- (2) It refutes, or is inconsistent with, a position the applicant takes in:

- (i) Opposing an argument of unpatentability relied on by the Office, or
- (ii) Asserting an argument of patentability.

A prima facie case of unpatentability is established when the information compels a conclusion that a claim is unpatentable under the preponderance of evidence, burden-of-proof standard, giving each term in the claim its broadest reasonable construction consistent with the specification, and before any consideration is given to evidence which may be submitted in an attempt to establish a contrary conclusion of patentability.

(c) Individuals associated with the filing or prosecution of a patent application within the meaning of this section are:

- (1) Each inventor named in the application;
- (2) Each attorney or agent who prepares or prosecutes the application; and
- (3) Every other person who is substantively involved in the preparation or prosecution of the application and who is associated with the inventor, with the assignee or with anyone to whom there is an obligation to assign the application.

- (d) Individuals other than the attorney, agent or inventor may comply with this section by disclosing information to the attorney, agent, or inventor.

(e) In any continuation-in-part application, the duty under this section includes the duty to disclose to the Office all information known to the person to be material to patentability, as defined in paragraph (b) of this section, which became available between the filing date of the prior application and the national or PCT international filing date of the continuation-in-part application.

[42 FR 5593, Jan. 28, 1977; paras. (d) & (e) - (i), 47 FR 21751, May 19, 1982, effective July 1, 1982; para. (c), 48 FR 2710, Jan. 20, 1983, effective Feb. 27, 1983; paras. (b) and (j), 49 FR 554, Jan. 4, 1984, effective Apr. 1, 1984; paras. (d) and (h), 50 FR 5171, Feb. 6, 1985, effective Mar. 8, 1985; para. (e), 53 FR 47808, Nov. 28, 1988, effective Jan. 1, 1989; 57 FR 2021, Jan. 17, 1992, effective Mar. 16, 1992; para. (e) added, 65 FR 54604, Sept. 8, 2000, effective Nov. 7, 2000]

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

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(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 3 is directed to a method for delivering a biologically active molecule into a cell comprising 1) covalently linking a molecule to the cell surface, wherein the molecule can act as a surface receptor, 2) complexing the biologically active molecule with a ligand for the surface receptor, and 3) contacting the biologically active molecule-ligand complex with the cell surface, whereby the biologically active molecule is delivered into the cell, wherein the covalently linked molecule is biotin and the ligand is avidin or streptavidin.

Claim 3 is rejected under 35 U.S.C. 102(b) as being anticipated by Wojda and Miller (Molecular Biology of the Cell, November 1997, Vol. 8, No. Suppl., p86A).

The contents of the meeting abstract are summarized as follows:

Endocytosis Mediated by Biotin-Avidin Crosslinking of Surface Proteins Does Not Require GPI-Proteins ((U. Wojda and J.L. Miller)) Laboratory of Chemical Biology, NIDDK, NIH, Bethesda Md 20892

Glycosylphosphatidylinositol anchored proteins (GPI-proteins) are abundant on all hematopoietic cells, and their clustering is associated with signal transduction and endocytosis. We tested the hypotheses that 1. general crosslinking of proteins on the exterior of cells leads to their endocytosis and 2. GPI-proteins are required for this process. Biotin-avidin (BA) crosslinking of the surface proteins in the absence of endocytosis was demonstrated on human red blood cells by flow cytometry and Western blotting. Endocytosis of fluorescein-labeled avidin was compared in native erythroleukemia K562 cells (GPI+) and a mutant cell line that does not express GPI proteins (GPI-). BA crosslinking did not affect K562 cells growth and viability as assessed by cell counting and dye exclusion. Fluorescent avidin was initially evenly distributed on the cell surfaces, but after 48 hours surface fluorescence was no longer detected. Internalization of the BA crosslinked surface proteins was observed within one hour and fluorescence signal was detected in the cells for six cell divisions. No internalization occurred at 4°C. No differences in the appearance of time course of BA mediated endocytosis between the GPI+ and GPI- K562 cells were noticed. In summary, BA crosslinked surface proteins on K562 cells undergo endocytosis and GPI-proteins are not required for this process.

In a telephonic interview with the examiner in response to a proposed Examiner's Amendment to cancel claim 3 and allow claims 9-10, and after having a copy of the relevant art faxed to her, applicants' representative asserted that the fluorescein molecule would not constitute a "biologically active" molecule as defined in the specification. This assertion is inaccurate. The specification teaches that a "biologically active molecule" means a molecule that, when introduced into a cell, can affect processes or reactions occurring within a cell (i.e. page 4, line 20 of the instant specification). In the Wojda and Miller Abstract, the biologically active molecule would be the fluorescein that is linked to avidin and transported into the targeted cell. After all, it is reasonable to expect that the targeted cells did not efficiently fluoresce prior to the introduction of the fluorescein into the cells. The examiner knows of no other way in which the experiments described above could have been performed without the covalent linkage of biotin to the cell surface (i.e. the covalently linked receptor).

Conclusion

Claim 3 is rejected. Claims 9-10 are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gerald G Leffers Jr., PhD whose telephone number is (571) 272-0772. The examiner can normally be reached on 9:30am-6:00pm.


If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel can be reached on (571) 272-0781. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Gerald G Leffers Jr., PhD
Primary Examiner
Art Unit 1636


GERRY LEFFERS
PRIMARY EXAMINER